

**REMARKS**

After entry of the amendment above, new claims 30-57 will be pending, and all previously pending claims (1-29) will be canceled. New claims 30-57 represent preferred embodiments of the claimed invention. Claims 30, 37, 44, and 51 are independent claims, with the differences between them being the progressive further definition of various moieties listed in the structure of claim 30. Briefly, claim 30 corresponds to now-canceled claim 27, although in claim 30, the structure of the HypNA/pPNA subunit is shown in the currently preferred manner. In claim 37, moieties  $R^6$ - $R^{11}$  of claim 27 have been defined to represent hydrogen atoms. In claim 44, moieties  $R^6$ - $R^{11}$ ,  $A^1$ , and  $A^2$  of claim 27 are also defined at the atomic level. Similarly, the structure in claim 51 atomically defines moieties  $R^6$ - $R^{17}$ ,  $A^1$ , and  $A^2$  of claim 27.

The foregoing amendments have been made to define certain preferred embodiments of Applicants' invention using currently preferred terminology and organization; not for reasons related to patentability. These amendments are supported by the specification and claims as originally filed, and they do not include new matter. Notwithstanding the amendments made herein, Applicants reserve the right to pursue subject matter no longer or not yet claimed here in this or one or more related patent applications.

With regard to Applicants' previously submitted Information Disclosure Statements, Applicants note that they are in the process of compiling copies of the references cited therein, and they will be provided as soon as they are all available.

Applicants respectfully request reconsideration of the invention as now claimed in view of the following additional remarks that concern the grounds of rejections set forth in the most recent Office Action.

1. 35 USC 112, First Paragraph, Rejection

Claims 27-29 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement, apparently because the specification did not set forth any experimental data to support the "assertion" that the compounds defined in the claims could be used to inhibit gene expression because, according to the Examiner, nucleic acid mimics require suitable conformations and flexibility, must be able to penetrate cell membranes, and bind targets with

the requisite specificity and affinity. While Applicants do not disagree with criteria set out by the Examiner with regard to nucleic acid mimics, they respectfully submit that experimental data is not required to enable their claimed invention. Rather than arguing over the matter, however, attached hereto as Exhibit A is a recent paper authored by Urtishak, *et al.* (Developmental Dynamics (2003), vol. 228: 405-413) that clearly demonstrates that compounds of the sort referenced in the claims can be used to practice the claimed methods. Specifically, the Urtishak, *et al.* paper describes several examples of the claimed methods, where oligonucleotide analogues according to the claims were used to "knock down" the expression of four different genes in zebrafish.

As the Urtishak, *et al.* paper clearly establishes, oligonucleotide analogues according to the invention can be used to inhibit gene expression in cells and organisms. Because the specification thus enables the subject matter of claims 30-57, the instant 35 U.S.C. 112, first paragraph, rejection should be withdrawn.

2. 35 USC 112, Second Paragraph, Rejection

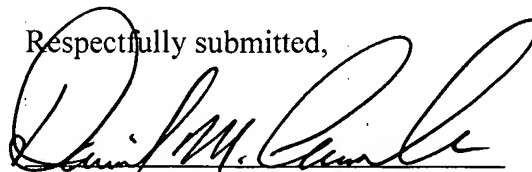
Claims 27-29 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite due to the listing of moiety R<sup>3</sup> in claims 27 and 29. As claims 27-29 have been canceled and since none of new claims 30-57 reference moiety R<sup>3</sup>, this rejection should be withdrawn.

**CONCLUSION**

Applicants respectfully submit that new claims 30-57 are in condition for allowance, and they earnestly solicit an early notice to such effect. Should any issues or questions remain, the Examiner is encouraged to telephone the undersigned at 858.350.9690 so that they may be promptly resolved without the need for an additional formal action and response thereto.

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Respectfully submitted,



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